UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,671	04/02/2007	Chris Dott	P71305US0	3706

136 7590 11/29/2007

JACOBSON HOLMAN PLLC
400 SEVENTH STREET N.W.
SUITE 600
WASHINGTON, DC 20004

EXAMINER	
FLOOD, MICHELE C	

ART UNIT	PAPER NUMBER
1655	

MAIL DATE	DELIVERY MODE
11/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,671	DOTT ET AL.	
	Examiner	Art Unit	
	Michele Flood	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/13/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of the receipt and entry of the amendment filed on June 5, 2006.

Claims 1-11 are under examination.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either an asserted utility or a well established utility.

Claims 1-10 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either an asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 provide for the use of a solid, semi-solid or liquid formulation of botulinum toxin for the preparation of a medicament intended to treat a disorder characterized by bladder spasms wherein said medicament is for administration without

using an injection into the bladder wall, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Objections

Claim 11 is objected to because of the following informalities:

There is an apparent misspelling in lines 2, 3 and 10 of Claim 11. Applicant may overcome the objection by replacing "characterised" with characterized.

There is an apparent misspelling in line 10 of Claim 11. Applicant may overcome the objection by replacing "patient" with patient.

There is apparent omission of an ampersand in line 13 of Claim 11. Applicant may overcome the objection by inserting and before "wherein" to place the claim in proper grammatical form.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Schmidt et al. (AF, WO 99/03483) and Dykstra et al. (AI, Dykstra, D. D. et al. Arch. Phys. Med. Rehabil., Jan 1990; 71: 24-26. Treatment of detrusor-sphincter dyssynergia with botulinum A toxin: A double-blind study.).

Applicant claims a method of treatment of a disorder characterized by bladder spasms, wherein the disorder characterized by bladder spasms is selected from the group consisting of urinary incontinence due to unstable bladder or unstable detrusor sphincter, voiding complications due to detrusor overactivity or unstable detrusor sphincter, urinary retention secondary to spastic sphincter or hypertrophied bladder neck and neurogenic bladder dysfunction secondary to Parkinson's disease, spinal cord injury, stroke or multiple sclerosis or characterized by a spasm reflex: wherein a patient requiring said treatment is administered with a therapeutically effective dose of a solid, semi-solid or liquid formulation of botulinum toxin, wherein said formulation is administered without using an injection into the bladder wall.

On page 11, line 20 bridging page 12, line 5, Schmidt teaches a method of treating a patient with urinary retention (incontinence) secondary to an injury sustained at the cervical vertebrae and characterized by a spasm reflex comprising administering to the patient 200 international units (IU) of botulinum toxin type A injections into the bladder neck for a total dose of 800 IU. Schmidt further teaches, "Peak bladder pressures pre-injection had been 200-cm water compared to post injection bladder pressures of 40 cm of water. The patient was continent with a penile clamp after treatment with botulinum toxin. In addition, walking and erections improved due to reduced bladder spasticity."

Dykstra teaches a method of treating a bladder spasm disorder comprising transurethral injection of effective amounts of botulinum toxin A into a bladder sphincter of a patient suffering from detrusor external sphincter dyssynergia secondary to a spinal

cord injury. Dykstra further teaches administering an initial dose of 140 units of toxin into three or four sites on the external urethral sphincter and subsequent injections of 240 units. See "*Materials and Methods*", on page 24-25, in its entirety.

The references anticipate the claimed subject matter.

Claim 11 is rejected under 35 U.S.C. 102(e) as being anticipated by Chancellor et al. (AD, US 2003/0108597 A1) and Doshi (AG, WO 2004/010934 A2).

Applicant's claimed invention was set forth above.

Chancellor teaches a method of treating bladder spasm disorders, *e.g.*, incontinence, voiding complications, urinary detrusor-external sphincter dyssynergia secondary to spinal cord injury or multiple sclerosis, hyperactive neurogenic bladder, spastic bladder, and bladder neck sphincter muscle spasticity, comprising administering to a subject lipid-based vehicles comprising a botulinum toxin (types A-G) via intravesical instillation, topical, spray, inhaler and oral administration in an amount effective to treat bladder contraction or bladder obstruction. *See* patent claims 46-59. *See* [0096] wherein Chancellor further teaches preparation of botulinum toxins as liquid solutions, suspensions, and solid forms for use in the making of the referenced delivery systems.

Doshi teaches intravesical administration of an effective amount of a botulinum to a patient in need thereof for the treatment of bladder spasm disorders, *e.g.*, detrusor instability, overactive bladder, neurogenic bladder and urinary incontinence, as well as urologic disorders including irritable, spastic, unstable, hypertonic, uninhibited,

dyssynergic and systolic bladder. *See* page 5, lines 9-20. On page 1, lines 27-30, Doshi describes detrusor hyperreflexia as a type of urge incontinence "which refers to an overactive detrusor muscle caused by neurologic disorders such as multiple sclerosis, Parkinson's disease, spinal cord injury, stroke, etc.". *See* page 5, line 21 to page 6, line 19, wherein Doshi teaches intravesical administration into the lumen of the bladder of suitable pharmaceutical forms of botulinum toxins (including toxin types A and B) via a suitable vehicle but excluding injection of the medication into the wall of the bladder. Non-toxic dose amounts of botulinum toxin delivered to patients are for example less than 3000 units for a 70 kg man, preferably between 1 and 1500 units and more preferably between 50 and 500 units per patient per treatment. Pharmaceutically acceptable forms include liquids, powders, creams (semi-solids), emulsions, suspensions and solutions, which can be delivered by use of a urinary catheter that extends into the bladder (*e.g.*, single-lumen catheter) or a multi-lumen catheter fixed to a balloon, or a suprapublic needle or catheter through the abdominal wall directly into the bladder, or a cytoscope, or a device for sustained release of the neurotoxin, or a compound comprising the toxin that adheres to the urinary tract or bladder mucosa, or a syringe, or an electromotive drug. *See* page 7, line 22 to page 9, line 31.

The references anticipate the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schmidt et al. (AF, WO 99/03483) or Dykstra et al. (AI, Dykstra, D. D. et al. Arch. Phys. Med. Rehabil., Jan 1990; 71: 24-26. Treatment of detrusor-sphincter dyssynergia with botulinum A toxin: A double-blind study.) or Chancellor et al. (AD, US 2003/0108597 A1) or Doshi (AG, WO 2004/010934 A2) in view of Suskind et al. (A*) and Ashton et al. (B*).

Applicant's claimed invention was set forth above.

The individual teachings of Schmidt, Dykstra, Chancellor and Doshi are set forth above. Neither Schmidt, Dykstra, Chancellor nor Doshi teaches a method of treatment characterized by bladder spasms comprising administering an effective amount of a botulinum toxin medicament to a patient in need thereof wherein the medicament is prepared in the form of a gel formulation. However, it would have been obvious to one of ordinary skill in the art to modify any of the methods of treatment taught by either Schmidt, Dykstra, Chancellor or Doshi to provide the instantly claimed invention because at the time the invention was made it was known in the art that botulinum toxin could be prepared as a gel, as evidenced by the teachings of Suskind and Ashton. For instance, Suskind taught that botulinum toxin could be prepared as a topical formulation in the form of a gel. Secondly, Ashton taught an implantable, injectable, or insertable, or otherwise administrable drug delivery composition that forms a hydrogel in a living tissue, and a method of using the composition to treat a living tissue in need of such

treatment. The drug delivery composition taught by Ashton comprises a codrug in admixture with a hydrogel-forming compound *in vivo*, which can be injected into or onto a living biological tissue without first forming the hydrogel prior to implantation, injection, insertion, or administration. Alternatively, the composition taught by Ashton can comprise a codrug combined a hydrogel-forming compound that may also be hydrated prior to injection, implantation, insertion, or administration. Codrugs used in the making of the pharmaceutical drug delivery composition taught by Ashton include anti-cholinergics. Given that Suskind taught that botulinum could be prepared as a medicament in the form of a gel and given that Ashton taught that anti-cholinergics could be used as a codrug in the making of the referenced *in vivo* hydro-gel forming compositions, one of ordinary skill in the art would have been motivated and one would have had a reasonable expectation of success to replace the pharmaceutical forms of the compositions comprising botulinum used to treat a bladder spasm disorder taught by either Schmidt, Dykstra, Chancellor or Doshi with a medicament comprising botulinum in the form of a gel formulation to result in the claimed invention because Suskind taught that compositions comprising botulinum in the form of a gel is a suitable vehicle for the delivery of the anti-cholinergic neurotoxin; and Ashton taught that the referenced hydrogel-forming compound may be mixed with an anti-cholinergic codrug for the delivery of the drug to patients in need of treatment with reduced side effects of toxicity and sensitivity to non-aqueous pharmaceutical carriers and increased stability and efficient delivery of the drug to the patient.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

* Applicant is advised that the cited U.S. patents and patent application publications are available for download via the Office's PAIR. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources. Should you receive inquiries about the use of the Office's PAIR system, applicants may be referred to the Electronic Business Center (EBC) at http://www.uspto.gov/ebc/index.html or 1-866-217-9197.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is 571-272-0964. The examiner can normally be reached on 7:00 am - 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MICHELE FLOOD
PRIMARY EXAMINER

Michele Flood
Primary Examiner
Art Unit 1655

MCF
November 25, 2007

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schmidt et al. (AF, WO 99/03483) or Dykstra et al. (AI, Dykstra, D. D. et al. Arch. Phys. Med. Rehabil., Jan 1990; 71: 24-26. Treatment of detrusor-sphincter dyssynergia with botulinum A toxin: A double-blind study.) or Chancellor et al. (AD, US 2003/0108597 A1) or Doshi (AG, WO 2004/010934 A2) in view of Ashton et al. (A*), Unger et al. (AC, US 2002/0099356 A1) and Unger (AE, 2003/0211975 A1).

Applicant's claimed invention was set forth above.

The individual teachings of Schmidt, Dykstra, Chancellor and Doshi are set forth above. Neither Schmidt, Dykstra, Chancellor nor Doshi teach a method of treatment characterized by bladder spasms comprising administering an effective amount of a botulinum toxin medicament to a patient in need thereof wherein the medicament is prepared in the form of a gel formulation or wherein the medicament is in the form of a solid, semi-solid or liquid botulinum toxin formulation spread on the outer wall of a balloon intended to be inflated inside the bladder. However, it would have been obvious to one of ordinary skill in the art to modify any of the methods of treatment taught by either Schmidt, Dykstra, Chancellor or Doshi by using either of the instantly claimed forms to provide the instantly claimed invention because at the time the invention was made the pharmaceutical forms were known in the art as pharmaceutically acceptable vehicles for the delivery of a medicament, as evidenced by the teachings of Ashton, Unger (AC) and Unger (AE).

Firstly, Ashton teaches

Secondly, Unger (AC)

Thirdly, Unger (AE)